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7 segment, at least one Jk segment, at least one human Ck segment, and a human 3' kappa
8 enhancer segment.

1 18. The construct of claim 17, wherein the human 3' kappa enhancer
2 segment is a 4 kb BamHI fragment containing the human 3' kappa enhancer.

1 19. A transgenic nonhuman mammal comprising the transgene of
2 claim 1.

1 20. The transgenic nonhuman mammal of claim 19, wherein the
2 transgene is expressed in B cells of the transgenic nonhuman mammal.

1 21. The transgenic nonhuman mammal of claim 19, wherein the
2 transgene is in the germline of the transgenic non-human mammal.

1 22. The transgenic nonhuman mammal of claim 19, further comprising
2 an Ig heavy chain transgene construct.

1 23. The transgenic nonhuman mammal of claim 21, wherein the
2 transgene is rearranged.

1 24. The transgenic nonhuman mammal of claim 21, wherein the
2 transgene is unrearranged.

1 25. The transgenic nonhuman mammal of claim 22, wherein the
2 transgene is rearranged.

1 26. The transgenic nonhuman mammal of claim 22, wherein the
2 transgene is unrearranged.

1 27. The transgenic nonhuman mammal of claim 19, wherein the
2 mammal makes an antibody response following immunization with an antigen.

1 28. The transgenic nonhuman mammal of claim 27, wherein the
2 antigen is a human antigen.

1 29. The transgenic nonhuman mammal of claim 27, wherein the
2 antibody response comprises a population of antibodies which comprise human μ chain-
3 containing immunoglobulins and human γ chain-containing immunoglobulins.

1 30. The transgenic nonhuman mammal of claim 20, wherein the B
2 cells produce a heterologous antibody.

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31. The transgenic nonhuman mammal of claim 30, wherein the B cells produce a population of heterologous antibodies of more than one isotype.
32. The transgenic nonhuman mammal of claim 19 wherein the nonhuman mammal is a rodent.
33. A method for generating a plurality of B cells expressing human antibody sequences, the method comprising:
providing a transgenic nonhuman mammal of claim 19; and
immunizing the transgenic nonhuman mammal to generate B cells producing a population of heterologous antibodies.
34. The method of claim 33, further comprising collecting the B cells producing a population of heterologous antibodies.
35. The method of claim 34, further comprising fusing the B cells producing a population of heterologous antibodies with immortalized cells to form hybridomas.
36. The method of claim 35 further comprising collecting the human antibody sequences from the hybridomas.
37. The method of claim 36, wherein the human antibody sequences are purified.
38. The method of claim 33, further comprising collecting the sequences encoding human antibodies.
39. The method of claim 38, wherein the sequences encoding human antibodies are full length.
40. The method of claim 39, further comprising expressing the sequences in a transfected cell.
41. A method of generating antigen-specific hybridomas secreting human sequence antibody, the method comprising:
immunizing the transgenic nonhuman mammal of claim 19 with a predetermined antigen;

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5 fusing lymphocytes from the transgenic mouse with immortalized cells to
6 form hybridoma cells; and
7 determining the binding of the antibody produced by the hybridoma cells
8 to the predetermined antigen.

1 42. A method for generating a human sequence antibody that binds to
2 a predetermined antigen, the method comprising the following steps:
3 immunizing the transgenic nonhuman mammal of claim 19 with a
4 predetermined antigen; and
5 screening hybridoma cells formed for the presence of antigen reactive
6 antibodies.

1 43. The method of claim 42, wherein the antigen reactive antibodies
2 are secreted from the hybridoma in culture.

1 44. The method of claim 42, wherein the antigen reactive antibodies
2 are substantially pure.

1 45. A method for producing rearranged immunoglobulin sequences
2 comprising:
3 providing the transgenic nonhuman mammal of claim 19;
4 obtaining the rearranged immunoglobulin sequences from the transgenic
5 nonhuman mammal.

1 46. The method of claim 45, wherein the obtaining step comprises
2 collecting B cell lymphocytes containing the rearranged immunoglobulin sequences from
3 the transgenic nonhuman mammal.

1 47. The method of claim 46, wherein the obtaining step comprises
2 isolating and amplifying mRNA from B cell lymphocytes to generate cDNA.

1 48. The method of claim 47, further comprising isolating and
2 amplifying heavy and light chain variable region sequences from the cDNA.

1 49. An isolated nucleic acid encoding the heavy and light chain
2 variable region sequences of claim 48.

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- 1 50. An isolated nucleic acid encoding the heavy chain variable region
2 sequences of claim 48.
- 1 51. An isolated nucleic acid encoding the light chain variable region
2 sequences of claim 48.
- 1 52. A vector comprising the nucleic acid of claim 49.
- 1 53. An expression vector comprising the nucleic acid of claim 49 in
2 which the heavy and light chain variable regions sequences of the nucleic acid are
3 operatively linked with a regulatory sequence that controls expression of the nucleic acid
4 in a host cell.
- 1 54. A host cell comprising the nucleic acid of claim 49, or progeny of
2 the cell.
- 1 55. The host cell of claim 54 which is a eukaryote.
- 1 56. The method of claim 45, further comprising:
2 culturing the host cell of claim 54 under conditions such that the nucleic
3 acid is expressed; and
4 recovering the nucleic acid from the cultured host cell or its cultured
5 medium.